

## Long-Term Memory and Aging A Cognitive Neuroscience Perspective

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There is little doubt that with age, long-term memory function declines. Countless behavioral studies have revealed significant differences in memory for lists of words (Smith, 1977), text (Dixon et al., 1982), contextual details (Park & Puglisi, 1985; Park, Puglisi, & Lutz, 1982), faces (Bartlett et al., 1989), abstract visual materials (Smith et al., 1990), and even television news (Frieske & Park, 1999). Although it is clear that memory decreases with age, there are a number of different views regarding the mechanisms underlying these age-related declines. Advances in neuroimaging have provided unprecedented opportunity to explore the neural underpinnings of behavioral theories of age-related memory decline and have resulted in new insights and neurally based theories accounting for memory phenomena associated with aging. In this chapter, we provide an updated view of what is known about aging and memory, integrating behaviorally based research with more recent neurally based findings.

Dominant views of causes of age-related declines in memory are varied in the cognitive aging literature. One broad theory is that there is a decline in processing resources, limiting the ability to encode and retrieve information. The clearest and perhaps earliest instantiation of this theory was presented by Craik and Byrd (1982). They argued that observed age-related declines in memory were caused by decreased "mental energy" or processing resource that limited the ability of older adults to engage in self-initiated processing. Later theorists have suggested that empirical measurement of processing resource could be represented by speed of information processing (Salthouse, 1994, 1996) or working memory capacity (Park et al., 1996, 2002; Salthouse et al., 1989; Salthouse & Babcock, 1991), both of which decline with age. Studies have conclusively demonstrated that both speed of processing and working memory mediate most, if not all, age-related variance in long-term memory

(Park et al., 1996, 2002; Salthouse & Babcock, 1991), demonstrating the utility of these constructs for understanding long-term memory.

In contrast to resource-based theories of speed and working memory, inhibition theory (Hasher & Zacks, 1988; Zacks & Hasher, 1997) suggests that older adults are less effective at gating or selecting information. Hence, they have less capacity available for effective encoding and retrieval of material, resulting in a long-term memory deficit. Other views of causes of memory decline with age include poor source memory (Johnson, Hashtroudi, & Lindsey, 1993), for which decreased ability to remember the context or source in which information is presented limits accurate recall of material with age.

Rather than focusing on age-related differences in difficulty recalling specific components of a memory such as context, Jacoby and colleagues (Jennings & Jacoby, 1993, 1997) suggested that there is an overall age impairment in recollection. They have argued that to understand age differences in memory, it is important to differentiate between memory processes that rely on explicit memory and memory based on feelings of familiarity. Jennings and Jacoby demonstrated convincingly that young adults rely on veridical explicit memory traces for memory performance, with some contributions from feelings of familiarity. In contrast, older adults' memory performance is dominated by automatically activated feelings of familiarity rather than explicit traces, resulting in degraded accuracy of their recall relative to young adults.

The connection of these cognitive theories of age-related decline in memory to neural function is one goal of this chapter, as is explicating new views of the aging memory that have resulted from neuroimaging studies. At the outset, it is important to note that the clarity and relative simplicity of behavioral theories are not mirrored in the neuroimaging literature. There are literally an infinite number of activation and deactivation patterns possible to be associated with memory function in a complex three-dimensional structure like the brain. Older adults may activate less, more, or even different neural structures to perform a memory task than young adults do (see Park et al., 2001; Cabeza, 2002; and chapter 2 of this volume for a more extended discussion of this issue). Further complicating interpretation of neural differences associated with aging on memory tasks are volumetric decreases in neural tissue that occur with age, with loss particularly marked in the frontal cortex (Raz, 2000; Raz et al., 1998). Nevertheless, despite these complications, neuroimaging studies have provided much insight into an understanding of aging and memory.

There are certain issues about memory that neuroimaging data are uniquely suited to answer. Behavioral measures of memory cannot ascertain if observed age differences result from strategy differences or mental effort exerted at encoding, as a result of differences in retrieval processes, or both. Neural activity, however, can be independently measured at encoding and retrieval, providing a unique window into processes that separately occur at these stages of memory.

In addition, neuroimaging allows a direct mapping of levels of activation in different brain sites to memory performance. Recall that Craik and Byrd (1982) suggested that decreased mental energy was the basis for age-related decline, which might lead one to expect consistently decreasing neural activation with age. However, neuroimaging studies suggest a different mapping. For example, Cabeza (2002) has argued that memory encoding and retrieval in older adults are often accompanied

by increased activation relative to young in the frontal cortex. Specifically, he suggested that hemisphere-specific activations in young adults may be reorganized in old age so that bilateral activation occurs, that is, there is relatively equivalent engagement of frontal cortex in the left and right hemispheres. As will be discussed, this pattern of hemispheric asymmetry reduction in older adults (HAROLD) has been reported in several studies of memory and aging and is a recurring pattern in studies of working memory (see chapter 8, this volume). Further explicating the difficulties in mapping views of cognitive resource to neural activation are studies that demonstrated that low elder performers (Cabeza et al., 2002; Rosen et al., 2002; Daselaar, Veltman, Rombouts, Lazeron, et al., 2003) and even patients with early Alzheimer's disease have higher levels of frontal activations than young adults during encoding (Lustig et al., 2003).

It is also important to keep in mind some of the unique methodological limitations imposed by neuroimaging techniques when studying memory. Perhaps the most serious issue is the response limitations that occur when cognitive processes are studied using positron emission tomography (PET) or functional magnetic resonance imaging (fMRI). When in the scanner, subjects are usually restricted to making a button press to indicate their memory for a stimulus. As a result, PET and fMRI studies overwhelmingly involve the use of recognition memory compared to recall. Yet, the self-initiated processing demands of recognition compared to recall are considerably attenuated (Craig & McDowd, 1987), so researchers are typically studying tasks for which age differences in memory performance are minimized.

A second problem with studying memory using neuroimaging is that neural differences between groups are most readily interpreted when behavioral performance is equivalent between the groups, yet the most reliable finding about memory and age is that older adults perform more poorly than young. Hence, studies often involve differences in both recall and neural activation, making the activations more difficult to interpret, or studies involve the relatively small subset of memory tasks that are not age sensitive. Activations in these tasks are interpretable, but may not reflect neural activity that would occur with age on more demanding memory tasks.

Another concern is that, to detect adequate neural signal, it is often necessary to present relatively lengthy memory lists. There is some evidence that older adults are disproportionately sensitive to interference in memory paradigms (Hedden & Park, 2001, 2003; May, Hasher, & Kane, 1999), and these unusually long lists could result in age-related interference aggregated with other types of memory effects.

In this chapter, we frame our review around encoding and retrieval processes, context memory, and the study of individual differences. As depicted in table 9.1, the most dominant memory process studied has been encoding, with fewer studies focused on retrieval and effects of contextual support. A few studies have examined individual differences, which we argue provide some of the most compelling evidence to date to interpret the often-contradictory findings present in the literature, particularly with respect to frontal activations.

The study of the cognitive neuroscience of memory and aging is in its infancy, and these early studies in some ways parallel behavioral studies of memory and aging from the 1960s and 1970s, which had a more functional rather than theoretical focus. At the same time, the window neuroimaging studies provides into age differ-

Table 9.1 Study Characteristics of Neuroimaging Articles on Long-Term Memory and Aging

Reference	PET	fMRI	Method	Type of Memory	Stage of Memory	Memory Test Format	Material Type
Grady et al., 1995	X			Intentional	Encoding	Recall	Word
Bäckman et al., 1997	X			Intentional	Encoding	Recall	Word
Schacter et al., 1996	X			Intentional	Encoding	Recall	Word
Cabeza, Grady, et al., 1997	X			Intentional	Encoding	Recall	Word
Grady et al., 1999	X			Intentional	Encoding	Recall	Word
Madden et al., 1999	X			Intentional	Encoding	Recall	Word
Cabeza et al., 2000	X			Intentional	Encoding	Recall	Word
Anderson et al., 2000	X			Intentional	Encoding	Recall	Word
Hidaka et al., 2001	X			Intentional	Encoding	Recall	Word
Logan et al., 2002	X			Intentional	Encoding	Recall	Word
Stebbins et al., 2002	X			Intentional	Encoding	Recall	Word
Grady et al., 2002	X			Intentional	Encoding	Recall	Word
Cabeza et al., 2002	X			Intentional	Encoding	Recall	Word
Rosen et al., 2002	X			Intentional	Encoding	Recall	Word
Daselaar, Veltman, Rombouts, et al., 2003	X			Intentional	Encoding	Recall	Word
Lazeron, et al., 2003	X			Intentional	Encoding	Recall	Word
Morcom et al., 2003	X			Intentional	Encoding	Recall	Word
Maguire & Frith, 2003	X			Intentional	Encoding	Recall	Word
Daselaar, Veltman, Rombouts, et al., 2003	X			Intentional	Encoding	Recall	Word
Park et al., 2003	X			Intentional	Encoding	Recall	Word
Lustig et al., 2003	X			Intentional	Encoding	Recall	Word
Cabeza et al., 2004	X			Intentional	Encoding	Recall	Word
Gutches et al., in press	X			Intentional	Encoding	Recall	Word

Note. fMRI, functional magnetic resonance imaging; PET, positron emission tomography.

ences in plasticity, strategy, and process is quite remarkable. These data are not only creating significant constraints for behavioral theories of aging, but are resulting in a tremendously fresh focus on new learning and strategy changes with age in the behavioral literature.

We also focus our review on neural activations in both frontal and hippocampal areas. Theorizing in the cognitive neuroscience of aging and memory has focused almost exclusively on frontal activation differences. The findings regarding age differences in engagement of the frontal cortex during memory processes are varied and often inconsistent. Cohen (Nyström et al., 2000; Miller & Cohen, 2001) has argued that neural resources can be deployed flexibly by the frontal cortex, so that inconsistencies could result from strategy differences between subjects, particularly in memory tasks for which there may be multiple routes to successful encoding and retrieval. Furthermore, shrinkage of the prefrontal cortex and localization of compensatory sites could vary because of individual differences with aging, leading to difficulty interpreting group results.

In addition to focusing on the role of the frontal cortex in age differences in long-term memory, we also focus considerable attention on the hippocampus and related medial temporal structures, which are critically important for encoding and associating novel information into memory (Stern et al., 1996; Brewer et al., 1998; Wagner et al., 1998; Cohen et al., 1999). We propose that, with age, memory function is characterized by (1) decreased engagement of the hippocampus and other medial temporal areas; (2) relatively reliable age differences in left frontal activations, with some studies showing heightened activity and others less activity with age; (3) bilaterality in the frontal cortex in older adults when young adults show unilateral activity. Similar to the confusing picture with respect to left frontal activations, age-associated bilaterality sometimes results from increases in activation of the nondominant hemisphere by older adults (Cabeza, Grady, et al., 1997; Bäckman et al., 1997; Madden et al., 1999; Grady et al., 2002; Logan et al., 2002; Rosen et al., 2002); it also occurs as a result of less activation in the old in the dominant hemisphere activated by the young (Logan et al., 2002; Stebbins et al., 2002). Whether bilateral activations with age are compensatory for less-efficient neural function with age is not a question that is easily answered. Important tests would show increased activation in the contralateral hemisphere as a function of within-subject difficulty conditions and more contralateral activation at encoding on items that were remembered compared to those that were forgotten.

## Encoding and Memory

There is a wealth of studies on the topic of encoding in both the behavioral and cognitive neuroscience literature of aging. Encoding has been isolated as a process that becomes impaired with aging because of numerous behavioral studies documenting age differences when subjects actively memorize materials (Smith, 1977) as well as under incidental conditions (Eysenck, 1974). There is good evidence that encoding is most impaired with age when the tasks demand substantial engagement

of cognitive resources and there are relatively few cues or environmental supports to guide encoding ( Craik, 1986; Park et al., 1990; Smith et al., 1998).

For example, Park et al. (1990) reported large age differences when old and young adults intentionally encoded pairs of unrelated pictures, but much smaller differences when the pictures were related because of more reliance in this last condition on world knowledge to support encoding and less reliance on basic processing mechanisms like speed and working memory. Similarly, Smith et al. (1998) found that elderly individuals integrate a target with a contextual cue effectively if there is a preexisting relationship among target and cue or an integration is provided by the experimenter. The elderly encounter difficulties with integration when the parts are seemingly unrelated, and they must engage in self-initiated processing, which draws heavily on cognitive resources.

## Early Neuroimaging Studies of Encoding Processes With Age

The first published study of neuroimaging and aging (Grady et al., 1995) involved PET scanning of face encoding in young and old adults. Presenting findings that ultimately would be reported by many subsequent investigators, Grady and colleagues found that, during encoding, younger adults engaged more left prefrontal cortex than old and showed increased activation in medial temporal areas. There was also a striking correlation between hippocampal and prefrontal activation present in the young (.94), but not the old (.02). Based on these findings, Grady et al. concluded that encoding in late adulthood was characterized by less neural activity and decreased connectivity between the frontal and hippocampal areas.

In another early study that involved words instead of faces, Cabeza, Grady, et al. (1997), using PET, neuroimaged intentional encoding of words in young and old adults. Like Grady et al. (1995), they also reported decreased left prefrontal activations in older adults; in addition, they noted roughly equivalent levels of activation in the old in the left and right prefrontal cortex (bilaterality), whereas young adults showed a focal, unilateral pattern of left frontal activations. The compensation hypothesis emerged from these data as Cabeza, Grady, et al. suggested that the observed bilaterality in the old could be caused by a compensatory recruitment of the right hemisphere as a result of inadequate activations in the left hemisphere.

The findings from these two initial, pioneering studies proved to be reliable, and the observations from these seminal studies continue to be the basis for much theorizing. The notion that the aging brain was not simply characterized by linear declines in activity was provocative and convergent with the theorizing and findings of Reuter-Lorenz and colleagues (2000) on working memory. In an astonishingly short period of time, it became nearly obligatory for behavioral researchers reporting on memory function to integrate their behavioral findings with these seminal studies and with later neuroimaging work on aging and memory.

Other early findings were suggestive of the engagement of qualitatively different neural networks to perform encoding tasks. Madden et al. (1999) studied intentional word encoding and reported that regression analyses of reaction times and regional cerebral blood flow indicated that left prefrontal activations predicted young but not older adults' reaction times. Rather, for old adults, reaction times predicted left

parahippocampal and right middle frontal activation, suggesting reorganization of neural systems with age. This conclusion was supported by a structural equation analysis of data from a PET study that also yielded evidence for reorganization of the neural systems in support of encoding and recall with age (Cabeza, McIntosh, et al., 1997).

### *Levels of Processing Manipulations at Encoding*

In the behavioral literature, there is conflicting evidence about the impact of "deep" processing at encoding on subsequent memory of items. When older adults are presented with orienting tasks that require them to make semantic judgments about stimuli, deep encoding is induced ( Craik & Lockhart, 1972). Generally, age differences persist under deep encoding and are of similar magnitude for incidental deep processing and intentional encoding (Eysenck, 1974; Smith, 1977; Simon, 1979; Mason, 1979), although there are exceptions for which deep encoding repairs older adults' memory to the level of young adults (Craik & Simon, 1980).

There are five neuroimaging studies of aging (Logan et al., 2002; Grady et al., 1999; Stebbins et al., 2002; Grady et al., 2002; Daselaar, Veltman, Rombouts, Raaijmakers, et al., 2003) that used levels of processing manipulations at encoding. All of these studies provided evidence for decreased activation of the left prefrontal cortex under intentional encoding compared to deep encoding, and all but one (Logan et al., 2002) showed evidence for decreased activations under deep-encoding conditions in the left inferior frontal cortex in old compared to young individuals; this area is associated with semantic processing (Demb et al., 1995; Poldrack et al., 1999). In addition, there is substantial evidence for decreased activation in older adults overall, as well as less medial temporal activation. Bilateral activations with age appear in many of the studies and generally occur as a result of less engagement of the left frontal cortex with age.

In an initial study, Grady et al. (1999), using PET, assessed the impact of shallow, deep, and intentional encoding of pictures and words in young and old adults. These investigators reported that young and old adults showed generally the same pattern of neural activations in response to the levels of processing manipulation, but that older adults' overall level of activation was attenuated compared to young adults. Deep encoding, when compared to intentional encoding, showed more activation of the left anterior prefrontal cortex and the hippocampus across subjects, but the old activated less in this area than the young. Interestingly, age differences in activation were larger for word encoding compared to pictures, just as memory differences as a function of age are larger for words than pictures. Because of the age differences in memory for words, it is not entirely clear whether the diminished neural activation drove poor memory or whether poor memory in older adults resulted in diminished activation.

In three subsequent levels of processing studies, deep encoding resulted in decreased left frontal activation in older adults compared to young adults. Stebbins et al. (2002) reported a study in which deep and shallow processing of words at encoding was examined in a young and old adult sample. They found evidence for increased activation in both old and young individuals under semantic-encoding condi-

tions. Congruent with the work of Grady et al. (1999), they reported decreased activation in left frontal areas in older adults compared to young adults during the deep semantic encoding condition. A bilateral activation pattern was observed in the frontal areas in old individuals, but it was because of decreased left frontal activation rather than an increase in right frontal activation above the level of young adults. In a later study, Grady et al. (2002) examined incidental shallow, incidental deep, and intentional encoding of faces, and as in the work of Stebbins et al. (2002), reported less left frontal activity in old individuals for deep encoding. There also was a correlation between frontal-hippocampal sites in young but not old adults, with a right prefrontal and parietal correlation in old adults. This finding demonstrated the use of different neural circuitry for task performance as a function of age and is suggestive of decreased hippocampal function in old adults. Finally, Daselaar, Veltman, Rombouts, Raaijmakers, et al. (2003) reported similar networks of activation in young and old individuals for a deep-processing task, with more left prefrontal activation and left hippocampal activation in young adults.

Thus, far, the studies reported are largely in agreement. The most global finding from these four levels of processing studies is that older adults remember less and show less neural activation. More specifically, the studies also demonstrated less left prefrontal activation in old individuals in semantic processing areas, particularly under intentional conditions.

In another study, using fMRI, Logan et al. (2002) studied encoding of words under three conditions: intentional memory, deep incidental processing (abstract vs. concrete judgments), and shallow incidental processing (temporal order of a letter). Behaviorally, both young and old showed a similar gain in memory for the items as a function of depth of processing. Memory was poorest for both age groups under phonemic encoding, intermediate for intentional encoding, and best for deep processing. Like the other studies described thus far, old adults had overall lower levels of activation across areas. Moreover, under intentional encoding conditions, as reported in the other studies, older adults showed less activation than young in left frontal cortex in Brodmann's areas 45 and 47, areas specialized for semantic processing (Demb et al., 1995; Poldrack et al., 1999).

The findings diverged from other studies in the deep-processing condition. Logan et al. (2002) reported that, under deep-encoding conditions, older adults showed left frontal activation at the same level as younger adults. They suggested that the difference in left frontal activations observed under intentional conditions between young and old was repaired or remediated by guiding older adults toward a deep encoding. Logan et al. also reported markedly less asymmetry of activation between hemispheres in old compared to young individuals, providing evidence for bilaterality. Logan et al. argued that older adults may have a production deficiency in use of strategies under intentional conditions, and that older adults are less selective in encoding operations in general. Older brains, however, activate more like younger brains under conditions of guided encoding for which strategies are controlled.

Superficially, it might appear that the Logan et al. (2002) findings are a fluke because four other studies found evidence for decreased left inferior frontal activations with age under deep-encoding instructions. However, in another study (also, like the Logan et al. study, conducted in the laboratory of Randy Buckner at Wash-

ington University, St. Louis, MO), Lustig et al. (2003) examined patterns of activation and deactivation in a large sample of young adults, healthy older adults, and older adults in early stages of Alzheimer's disease. This is not a true level-of-processing study because subjects only encoded words under deep-processing conditions. Nevertheless, these data are highly relevant to the issue of left frontal activations with age under deep-encoding conditions. As shown in figure 9.1a, Lustig et al. reported striking evidence for increased activations by both healthy and demented older adults in the left frontal cortex compared to young adults under deep-encoding conditions. The finding of equivalent or even higher levels of activation in older adults in left frontal areas under deep encoding is almost certainly reliable because the Lustig et al. (2003) study has one of the largest *n*'s of studies to date (27 healthy old and 23 demented old), and the time course analysis displayed in figure 9.1 shows differences were maintained as a function of age over approximately a 25-s presentation block.

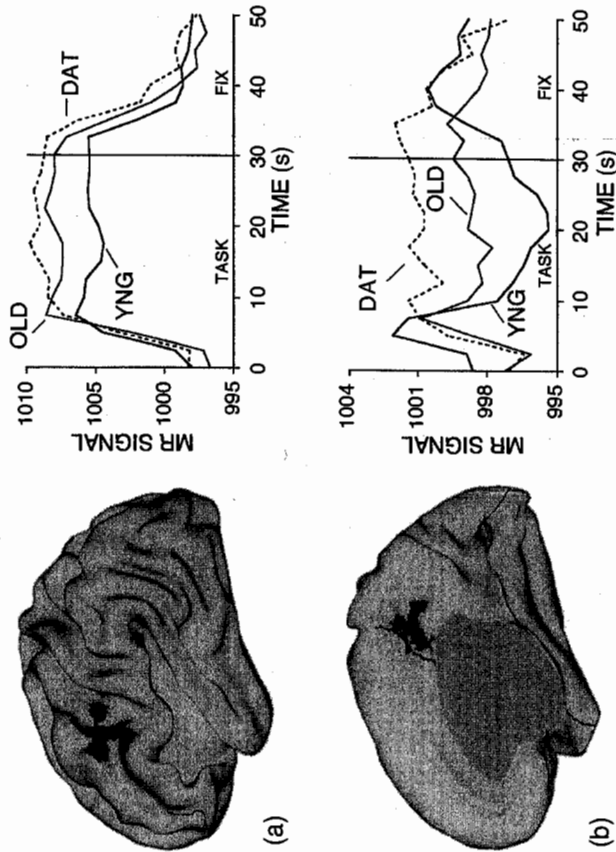


Figure 9.1. *a*, The activation and time course for left inferior frontal cortex. (from Lustig et al., 2003.) Note that both healthy and demented older adults showed increased activation compared to young (YNG) adults under deep-encoding conditions, and that activation was maintained over the entire task block before dropping off during fixation. *b*, Activations and time course for medial parietal/posterior cingulate cortex. Patients with dementia of the Alzheimer type (DAT) activated this region more than healthy elderly, who activated the region more than the young. (From "Adult Age Differences in Functional Neuroanatomy of Verbal Recognition Memory," by C. Lustig et al., 2003, *Proceedings of the National Academy of Sciences USA*, 100, 504–514. Copyright 2003 National Academy of Sciences, U.S.A.)

The data on levels of processing provide an inconsistent picture of encoding differences in neural activations as a function of age. Generally, the studies found consistent evidence for bilaterality in older adults, but it was often caused by decreased activation of the left frontal cortex relative to young adults rather than increased engagement beyond the level of younger adults, so it is harder (but not impossible) to make a compensation argument for this pattern than for a pattern in which activation increases above the level of young adults. Moreover, the data suggesting increased activation in left frontal areas in mildly demented subjects might be taken as evidence of a disinhibition or decreased selectivity rather than for the compensation argument, but it could also plausibly be that subjects with the poorest neural function showed the most activation, thus arguing that the pattern is supportive of compensation.

We believe that to reconcile whether deep encoding is characterized by more or less left frontal recruitment and whether the frontal recruitment is compensatory, it is important to demonstrate encoding conditions within subjects that increase or decrease engagement of left frontal areas in older adults. Relating such changes in frontal engagement to performance as well as to individual differences of subjects will bring much clarity to the issue of deep processing, aging, and left frontal activation.

The results of level-of-processing manipulations on medial temporal function are somewhat clearer. Of the three studies that examined activations in medial temporal areas, all reported some age differences in the role of the hippocampus in intentional versus deep incidental comparisons (Grady et al., 1999), deep versus shallow incidental encoding comparisons (Daselaar, Veltman, Rombouts, Raaijmakers, et al., 2003), or correlations of the hippocampus with behavior (Grady et al., 2002).

Finally, a methodological point worth noting is that, in a number of the studies (Stebbins et al., 2002; Daselaar, Veltman, Rombouts, Raaijmakers, et al., 2003), memory was not assessed or not reported. Future studies should include memory outcome measures because, without behavioral measures, it is difficult to interpret activation patterns, and actually, if there are no memory measures, it is uncertain whether these encoding conditions should be considered as memory studies. In closing this section, we should also note that the reports of the effects of deep versus intentional processing on memory in older adults in the behavioral literature are quite variable (see Kausler, 1990, for a review). Although the level-of-processing effect has proven to be one of the most reliable and integrative for the study of human memory, models that address changes in the quantity or engagement of processing resource with age have not been the most informative in understanding aging memory (e.g., Craik, 1986; Hasher & Zacks, 1979; see reviews in Hasher & Zacks, 1988, and Park, 2000). Hence, we suspect that confusion about engagement of neural resources will not be resolved by studying the depth of processing manipulations.

### Differences in Encoding of Remembered Items

Since the seminal Grady et al. article on memory and aging was published in 1995, techniques for measuring neural signal have evolved. Event-related fMRI allows accurate recording of signal with a temporal resolution of as little as 2 s for whole

brain coverage. Event-related designs are particularly useful for the study of memory because neural events associated with successful versus unsuccessful encoding of individual stimuli can be measured.

Using fMRI, Wagner et al. (1998) recorded event-related signal during encoding of words. Then, based on out-of-the-scanner recognition performance for the words, they sorted successfully encoded items (those recognized with high confidence) from those forgotten (those that were missed). The findings revealed that subjects were more likely to engage the parahippocampal gyrus for remembered compared to forgotten items, a finding also reported for pictures by Brewer et al. (1998).

There are three studies to date in the aging literature (Morcom et al., 2003; Daselaar, Veltman, Rombouts, Lazeron, et al., 2003; Gutchess et al., in press) that have used the subsequent memory paradigm to examine the neural signal at encoding associated with items that are remembered. These studies are particularly important as they may potentially provide insight into the difficult arguments regarding the relationship between heightened activation levels and compensation in older adults. If greater activation with age is compensatory, it would be expected to see more bilaterality and greater activation above perhaps young baseline levels for remembered versus forgotten items. Thus far, the findings are somewhat variable, with two of the three studies showing some evidence for decreased medial temporal activation for remembered items in old individuals and a mixed picture for frontal areas.

Morcom et al. (2003) studied word memory using an incidental, deep-processing task. When forgotten items were subtracted from remembered items, young and old adults showed equivalent levels of activation in the left inferior frontal cortex, supporting the findings of Logan et al. (2002) for deep processing. Old individuals showed enhanced activity for forgotten items compared to remembered items and, on query of frontal cortex in a regions-of-interest analysis, more bilateral anterior prefrontal activation for remembered items compared to young. Whether this additional recruitment is compensatory or merely decreased selectivity of encoding for old adults cannot be determined from the pattern of findings. In addition, both groups showed more hippocampal engagement for remembered items, although young individuals showed more activation of the left anterior inferior temporal cortex for remembered compared to forgotten items than old adults.

Daselaar, Veltman, Rombouts, Lazeron, et al. (2003) conducted a similar study, but due to an inadequate number of misses they compared remembered items to baseline rather than to forgotten items. Unlike Morcom et al. (2003), they observed equivalent amounts of lateralization between old and young individuals. The most interesting finding was related to hippocampal activation and occurred when older adults were divided into high-performing and low-performing memory groups based on recognition performance. The old-low individuals showed less medial temporal activation for remembered items than either old-high or young adults.

Finally, Gutchess et al. (in press) examined memory for pictures in an incidental deep-processing task. They reported more parahippocampal activation in young adults compared to old for remembered items, even when subjects were not divided into high and low performers. They also found significantly more recruitment of the left frontal cortex in old adults compared to young adults for remembered items. Given that pictures generally induce bilateral prefrontal activations (Kelley et al.,

1998), the older adults' increased recruitment of the left prefrontal cortex above the level of young adults suggests a selective activation that is potentially compensatory.

The subsequent memory paradigm is a potentially rich tool that, with sufficient  $r$ 's and varied encoding conditions, may permit disentangling functional from dysfunctional neural signal. At present, the findings have not yielded the clarity that one would hope for, but we believe that event-related designs that can separate the neural signal associated with remembered items from forgotten items offer a powerful tool that will yield a better understanding of memory function in late adulthood, particularly when individual differences in cognitive performance are examined, as demonstrated by Daselaar, Veltman, Rombouts, Lazeron, et al. (2003). Sorting remembered from forgotten items provides specificity at the level of process, and differentiating subjects based on cognitive performance provides specificity at the level of ability.

We should note that two of the three studies provided some evidence for decreased medial temporal activation with age for remembered items. The hippocampus is the primary structure that deteriorates with Alzheimer's disease. Alzheimer's disease is a ubiquitous disorder in later years; about 40% of older adults aged 85 years and older have frank Alzheimer's disease (Kukull et al., 2002; Launer et al., 1999). Given the disorder's long and slow progression, it is very plausible that decreased hippocampal activations in older adults may reflect early-stage Alzheimer's disease. If this is the case, apparent age differences in this region would be driven by a subset of subjects. The differences between old-high and old-low individuals found by Daselaar, Veltman, Rombouts, Lazeron, et al. (2003) are consistent with such an explanation.

### Nonverbal Stimuli

The study of meaningful pictures is an ideal medium for understanding age differences in neural circuitry and potentially compensatory neural processes in older adults because it is often possible to equate performance between old and young adults on picture memory tasks (Park, Puglisi, & Smith, 1986; Park et al., 1988; Smith et al., 1990), permitting a clear interpretation of different patterns of neural signal. Moreover, the encoding of relational elements within meaningful scenes is particularly demanding of the hippocampus (Cohen et al., 1999; Stern et al., 1996), providing a strong medium for assessing medial temporal as well as frontal function in older adults. There are several studies that have used pictorial stimuli with older adults, and overall they present a strong picture of decreased hippocampal function with age, with a more variable pattern for frontal activations.

Grady et al. (1999) directly contrasted pictorial and verbal memory in young and old adults, presenting line drawings of objects as well as words for study. Generally, old adults showed similar patterns of neural circuitry, but decreased activation relative to young in frontal and medial temporal areas. The exception was a contrast between deep and shallow processing for pictures, for which older and younger adults showed relatively similar levels of activation increases in left prefrontal and medial temporal regions. It is important to note that these were line drawings of simple objects and probably made low demands on relational processes in the hippo-

campus. In a study of facial memory, Grady et al. (1995) reported less left prefrontal and medial temporal activations in old compared to young adults for encoding of faces; a later study suggested that the reduced activations in old individuals may occur primarily during shallow encoding and recognition processes rather than deep encoding (Grady et al., 2002).

Other work has focused exclusively on pictorial stimuli. Iidaka et al. (2001) examined neural activations when young and old adults encoded related and unrelated pictures as well as abstract pictures. Young adults showed bilateral activations in the prefrontal cortex for concrete unrelated pictures and abstract pictures, conditions more demanding of resource than the related picture condition. Overall, old adults showed lower activation levels than young for the unrelated and abstract pictures, with the main difference in the temporoparietal areas. Iidaka et al. noted that older adults showed significant left prefrontal activations, suggestive of intact semantic processing, and had particular decreases in temporoparietal activations, indicative of deficient visuospatial processing.

Decreased medial temporal activations were also observed during pictorial encoding in young and old adults by Park, Welsh, et al. (2003) in an event-related design. They reported significantly less left anterior hippocampal engagement in older adults compared to young during encoding. Older adults, however, showed heightened left and right frontal activations on a subsequent probe task that occurred after each encoding event, which may have been compensatory for the decreased hippocampal activation.

Gutchess et al. (in press) provided a fine-grain understanding of pictorial encoding operations in older adults by utilizing a subsequent memory paradigm for the encoding of complex pictures in young and old adults. As described in the subsequent memory section of this chapter, they reported that young and old adults showed bilateral prefrontal activations for remembered compared to forgotten pictures. However, older adults showed a somewhat different pattern in other regions, recruiting more left middle frontal cortex than young adults as well as showing less parahippocampal activation. The finding of increased left frontal activation in old individuals might be compensatory. It replicates findings from visuospatial studies in other domains, as Reuter-Lorenz et al. (2000) also reported increased left frontal activations for the maintenance of nonverbal materials in working memory. Moreover, Park, Welsh, et al. (2003) also found increased left and right frontal activations for old adults in a probe task following pictorial encoding.

To summarize, the literature on neural activation associated with pictorial encoding suggests that older adults show less engagement of medial temporal areas than young adults; this region has been strongly implicated in processing relationships among elements of meaningful scenes. Second, there were several studies showing age-equivalent activations in frontal areas under at least some conditions (Grady et al., 1999, 2002; Iidaka et al., 2001) and even some studies showing increased frontal activation for remembered pictures at encoding (Gutchess et al., in press). Finally, increased frontal function in old adults in studies of pictorial memory has most frequently occurred when meaningful scenes have been presented (Park, Welsh, et al., 2003; Gutchess et al., in press). Whether these increased frontal activations are indicative of compensatory activation cannot be determined from the findings and is

an important area for future investigation. Evidence is accumulating to suggest that activations in medial temporal regions are decreased in old compared to young individuals (Grady et al., 2002; Gutchess et al., in press), and we speculate that the increased activation observed in other regions may be compensatory for the decreased medial temporal function.

### *Divided Attention at Encoding*

Much of our everyday encoding processes occur against a background of distraction and ongoing activity. Moreover, we frequently perform or attempt to perform two or more tasks at the same time. Hence, an understanding of how encoding processes function in the context of distracting activity is an important issue to characterize memory effectively. There is strong evidence from the behavioral literature that encoding processes that occur when distracting tasks or information are present are more disadvantaged by age than retrieval processes (Anderson, Craik, & Naveh-Benjamin, 1998; Craik et al., 1996; Park et al., 1989). Hence, different age patterns of neural activation between divided and full-attention conditions might be expected.

Anderson et al. (2000) studied encoding of word pairs while subjects were making tone discriminations. They found that the divided attention task reduced memory equivalently in young and old adults and reduced left prefrontal and medial temporal activations at an equivalent level in young and old adults. Anderson et al. concluded that these data are confirmatory of the age encoding deficit hypothesis advanced by Craik (1986) because both age and divided attention decreased left prefrontal activations during encoding, suggesting that shared mechanisms are operating in these two conditions.

### **Retrieval and Memory**

Older adults almost universally report problems with retrieval from both semantic and episodic memory. Nevertheless, the behavioral literature suggests that retrieval is much less impaired with age than encoding. Both Anderson, Craik, and Naveh-Benjamin (1998) and Park et al. (1989) demonstrated that older adults are disproportionately disadvantaged by interference at encoding but not retrieval when compared to younger adults. Craik et al. (1996) demonstrated a similar phenomenon and were able to show the automatic, obligatory nature of the retrieval operation—an operation that remains relatively unimpaired with age.

### **Neural Activations at Retrieval**

There is a substantial body of literature on age differences in neural activation at retrieval. The HERA (Hemispheric Encoding/Retrieval Asymmetry) model suggests that retrieval is largely a right hemisphere activity (Tulving et al., 1994). Overall, age differences in neural activations at retrieval are most consistently focused on frontal areas, with medial temporal differences appearing less often. In an initial

study, Grady et al. (1995) found that young individuals showed right prefrontal activity, as well as right parietal and bilateral occipital activations, when recognizing encoded faces, confirming the HERA model. Older adults also showed right prefrontal activations, but no significant activations in the other regions exhibited by the young. In addition, they reported a correlation of .94 between the activity in the frontal cortex and right hippocampal activity for young adults, but no relationship for older adults ( $r = .02$ ).

These findings were replicated in a later study (Grady et al., 2002) and are suggestive of different retrieval networks with age, with young adults relying more on hippocampal circuitry than old adults. Madden et al. (1999) also confirmed the finding of engagement of different networks for recognition in old compared to young individuals. In this study, regression analyses of reaction time to regional cerebral blood flow suggested that memory retrieval networks encompass more regions (specifically in posterior cortex) in elderly adults. Thus, these studies suggested that retrieval may involve a qualitatively different neural network in old compared to young people.

### Difficulty and Effort Manipulations at Retrieval

Behaviorally, performance differences as a function of age become larger as tasks require more directed retrieval (Light, 1991). For example, age differences are larger for explicit compared to implicit memory (LaVoie & Light, 1994; Park & Shaw, 1992) and for recall compared to recognition (Craig & McDowd, 1987; Rabinowitz, 1984, 1986; Schonfield & Robertson, 1966). Bäckman et al. (1997) measured neural activations in a PET scanner in young and old adults under different memory conditions. In the explicit condition, subjects were instructed to complete letter stems with studied words and with the first word that came to mind that completed the letter stem in the implicit condition. During explicit retrieval, both young and old adults showed increased activation of right prefrontal cortex when contrasted with implicit performance. Young adults showed unique activations as well in Wernicke's area and the left cerebellum for explicit retrieval, but the overall pattern was one of similar engagement of frontal systems for retrieval in young and old adults.

Cabeza, Grady, et al. (1997) conducted, using PET, one of the few studies contrasting verbal recall with recognition. They found decreased activation in the right frontal cortex with age, resulting in a pattern of bilateral activation for old and a more unilateral pattern for young adults. In addition, differences in activation patterns between recall and recognition were larger for young compared to old adults, suggesting less differentiation of neural activity in old individuals as a function of retrieval condition.

Schacter et al. (1996) varied how well subjects learned words at encoding for young and old adults. Using PET to image retrieval for the words, Schacter et al. found old and young individuals had equivalent hippocampal activations, and that these activations increased for better encoded words. Prefrontal activations, however, differed, with young adults showing typical increases in the anterior frontal cortex during retrieval, whereas older adults showed a more posterior pattern of frontal

recruitment. This again supports the conclusion that older adults engage different networks at retrieval than young adults, although it is not clear whether the differential engagement reflects strategy differences or neural reorganization.

Anderson et al. (2000) manipulated divided attention at retrieval in young and old adults following the encoding of word pairs. They reported that divided attention had little effect at retrieval on either old or young adults, reflecting the obligatory nature of the retrieval process.

Finally, Daselaar, Veltman, Rombouts, Lazeron, et al. (2003) presented a pattern of findings that potentially account for inconsistencies in activation patterns among studies. They studied retrieval following semantic encoding of words and reported a pattern of decreased frontal activity in older adults. A split of high and low performers within the old group, however, revealed that low-performing elderly showed more prefrontal activations than young adults, whereas high-performing elderly showed the least, suggesting that disparate findings can be reconciled via the study of individual differences.

In general, neural patterns associated with episodic retrieval showed less-dramatic differences between old and young than encoding studies. Moreover, all studies noted frontal decreases, with considerably less evidence for hippocampal differences than is true in the encoding literature. Finally, there was considerable evidence for engagement of different networks with age, but whether these reflect neural reorganization or strategy differences is not clear from the present studies.

### Recognition of Autobiographical Memories

Maguire and Frith (2003) examined the role of personally relevant information in recognition for young and old adults. They collected information from each subject regarding memory for specific autobiographical and public events prior to an experimental session and designed stimuli that were unique to the individual subject for presentation in an fMRI study. An intriguing pattern of age-related changes in hippocampal activations occurred. They found that elderly adults recruited the hippocampi bilaterally for autobiographical event retrieval trials, whereas young adults showed left-lateralized activations. Unlike the encoding studies reviewed, this study suggested that conditions do exist in which elderly adults activate the hippocampus more than young. Personally relevant or emotional information is likely part of an elaborate semantic network and may be less fragile than purely experimental/episodic information, thus eliciting robust hippocampal activations. Understanding whether rich, elaborated memories show different activation patterns than less-elaborated traces, at both encoding and retrieval, is an important issue for future research.

### Context and Memory

There is a large body of behavioral literature on the benefits of contextual materials at encoding. In fact, some theorists argued that poor memory for contextual or source information is a fundamental mechanism accounting for poor memory in older adults (Johnson, Hashtroudi, & Lindsay, 1993). Findings indicated that older adults show

larger differences for context memory than for item memory (Park & Puglisi, 1985; Park, Puglisi, & Lutz, 1982; Spencer & Raz, 1995) and have problems in binding target to context (Chalfonte & Johnson, 1996). Other behavioral work has focused on the potentially supportive role of context at encoding and retrieval and the working memory requirements of utilizing context. In paired associate tasks, when a target is unrelated to context and requires active integration and engagement of working memory, age differences are larger than when the context automatically activates an association through semantic relationships (Park et al., 1990; Smith et al., 1990, 1998).

At this point, there are only a few studies that have examined age differences in neural activations underlying contextual manipulations. Iidaka et al. (2001) studied age differences in encoding pairs of related and unrelated pictures. Both young and old adults showed increased left prefrontal activation for unrelated pictures compared to the control condition, reflecting the increased processing demands of utilizing the unrelated pictures as cues. At the same time, older adults showed less activation than young adults in right occipitotemporal areas, suggesting that they were less likely to encode the visuospatial features of the stimuli. No significant frontal activations were observed for young or old adults in the related-item condition, reflecting the relatively automatic encoding of related items; another possible cause is that the power in this study was low, even by imaging standards, with only seven subjects in each age group.

Two other studies of aging and context focused on retrieval of contextual information. First, Cabeza et al. (2000) used PET and studied item and order memory associated with the encoding of words. They reported that young adults showed increased activation in the right prefrontal cortex for order information compared to item information, whereas older adults did not, exhibiting less engagement of frontal areas in old compared to young individuals. This finding is consistent with reports of more impaired memory for context relative to item memory with age (Spencer & Raz, 1995). It is important to note as well that a pattern of activation suggestive of compensation for order information was observed in older adults. They showed weaker activations in the right prefrontal cortex compared to young adults, but greater activation in left prefrontal areas.

In a later study, Cabeza et al. (2002) presented subjects with words that were spoken aloud or presented visually and then measured neural activation at recognition for items and source. They again found that young adults showed lateralized activations in the right prefrontal cortex for source trials. High-performing, but not low-performing, old adults had bilateral activity in prefrontal areas, a finding consistent with compensatory activations in old individuals.

The data on utilization and memory for context are relatively sparse in the imaging literature. Cabeza et al. (2002) yielded patterns of compensatory, bilateral activation in high-performing old adults for contextual retrieval relative to young individuals, but the Iidaka et al. (2001) study, which focused on encoding, did not show a compensatory pattern and found decreased activations primarily in ventromedial temporal areas. Clearly, more studies are needed in the imaging literature on feature and contextual memory, particularly at encoding. We have a poor understanding of strategic differences for utilization of contextual information by older

adults at encoding and the support that context may provide at retrieval. Neuroimaging studies have the potential to provide great insight into strategy differences at encoding and context utilization differences between young and old adults at both encoding and retrieval.

### Individual Differences and Memory

Cognitive aging researchers have frequently used individual differences in various characteristics among subjects to explain sources of variance in memory function. For example, Lindenberger and Baltes (1994; Baltes & Lindenberger, 1997) reported that individual differences in sensory function (audition and vision) mediated substantial variance on a long-term memory task. Park et al. (1996, 2002) found that individual differences in speed and working memory accounted for age-related variance on many types of long-term memory tasks, including free recall, cued recall, and spatial recall. The importance of education and social context in response to environmental support has also been studied (Craik, Byrd, & Swanson, 1987; Cherry & Park, 1993). Work has even demonstrated that individuals' variability in performance on free-recall tasks over days may be an important predictor of later cognitive decline (Hultsch et al., 2000; Li et al., 2001).

Although the data on individual differences as predictors of patterns of neural function associated with memory are limited, the study of individual differences is a very powerful technique for understanding conflicting findings across studies. Characterizing subjects through neuropsychological batteries may provide substantive insight into the functional significance of different activation patterns. To the extent that bilateral patterns of activation are associated with good performance, it would suggest that recruitment of two hemispheres is likely compensatory for declining neural efficiency (Cabeza, 2002; Cabeza et al., 2002; Rosen et al., 2002).

On the other hand, if memory performance is poorer in individuals showing bilateral patterns of activation, the meaning of the pattern becomes somewhat harder to interpret. It may be that only low-memory subjects show bilateral recruitment patterns because only these subjects need the additional neural resources to perform the task (see the Daselaar and Cabeza walking stick argument in chapter 14 of this volume). At the same time, perhaps poor subjects are more disinhibited or increased activation is a marker of cognitive dysfunction. Note that the data presented in figure 1 of Lustig et al.'s 2003 work could support either argument.

At this time, there are six studies (Cabeza et al., 2002; Rosen et al., 2002; Logan et al., 2002; Lustig et al., 2003; Stebbins et al., 2002; Daselaar, Veltman, Rombouts, Lazeron, et al., 2003) relating individual differences in cognitive performance to patterns of neural activation. Of these, two suggested that bilateral activation patterns are associated with good performance; the other four reached the opposite conclusion. Cabeza et al. (2002) separated low- and high-memory subjects based on a battery developed by Glisky, Polster, and Routhicaux (1995). They imaged source retrieval using PET and reported that high-functioning old adults showed bilaterality, but that lower functioning old individuals exhibited changes in activation within sites in a single hemisphere. Cabeza et al. argued that contralateral recruitment in

older adults is reflective of neural modification and reorganization over time to compensate for declining structural integrity of the nervous system.

In support of this finding, Rosen et al. (2002) also reported that older subjects who scored highly on a memory battery outside the scanner showed not only the typical left prefrontal activation pattern, but also greater right prefrontal activation than young adults. In contrast, low-performing elderly showed reduced activations in both left and right frontal regions.

These findings are generally supportive of a compensation view (Cabeza, Grady, et al., 1997; Cabeza et al., 2000, 2002; Cabeza, 2002). Unfortunately, other studies that have related individual differences in performance to patterns of neural activation yielded the opposite conclusion, that is, that bilaterality is more characteristic of poor performers. Logan et al. (2002) reported that bilaterality of the frontal cortex across a number of different encoding conditions was most likely to be evidenced by the oldest adults, whereas young adults and the younger subset of older adults showed a more selective (unilateral) recruitment pattern.

In a follow-up study, Lustig et al. (2003) considered healthy old and old adults in early stages of Alzheimer's disease. As displayed in figure 9.1a, both groups showed increased left frontal activation during encoding of words, suggesting increased activation in this area was characteristic of aging. More important for the present issue, however, is that there were differences between the healthy elderly and patients with early Alzheimer's disease in the medial parietal/posterior cingulate cortex (figure 9.1b). In this area, patients with Alzheimer's disease displayed more activation during encoding than healthy elderly, and healthy elderly exhibited more activation than young adults. This pattern of findings is strongly suggestive of increased activation as dysfunctional, although note that these activations were outside the prefrontal cortex. Perhaps activations in some frontal areas are compensatory for old individuals, and other areas are dysfunctional. We recognize, of course, that the argument cannot be ruled out that additional recruitment, such as that displayed in figure 9.1b, occurs because of its compensatory value for neural deterioration in patients with Alzheimer's disease.

Also reporting evidence for increased activation in poor performers, Stebbins et al. (2002) found that decreased performance on neuropsychological tests was correlated with decreased frontal lobe activation on a deep-encoding task, and that bilaterality in old adults resulted from reduced left hemisphere activation rather than increased right hemisphere activation.

Finally, Daselaar, Veltman, Rombouts, Lazeron, et al. (2003), using an incidental deep-encoding task followed by retrieval, separated subjects into old-high and old-low performers based on memory performance in the scanner. At encoding, old-high and young individuals showed greater medial temporal activations than old-low adults and relatively equivalent activation and lateralization of frontal activity. At retrieval, old-low adults exhibited widespread greater activation, although these differences vanished when only correct responses were included in the analysis.

How can these findings be reconciled? There is no apparent consistent thread to manipulations used in the studies. Of the four studies reporting evidence that high activation or bilaterality is characteristic of low performers (Daselaar, Veltman, Rombouts, Lazeron, et al., 2003; Logan et al., 2002, Lustig et al., 2003; Stebbins et

al., 2002), all used deep-encoding tasks, but so did a study finding evidence for compensatory bilaterality (Rosen et al., 2002). The relationship of encoding and retrieval operations is also unclear because compensation was found in one encoding and one retrieval study even though all four studies that found evidence for dysfunctionality of increased recruitment studied encoding.

What is clear is that heightened activation in frontal areas relative to young individuals is significant for understanding the cognitive neuroscience of aging, and that there are conditions under which the activation is functional and others for which it is dysfunctional. It seems likely that carefully characterizing large numbers of subjects on multiple imaging and behavioral memory tasks, as well as relating performance to other domains of cognition such as attention and working memory, will provide tremendous insight into these provocative and important relationships.

## Conclusions

At the end of each section of this chapter, we summarized findings and recommendations for future research in particular domains. We now adopt a broader view and conclude by addressing two issues. First, how consistent are current behavioral theories of memory with extant neuroimaging data? Second, how do neuroimaging findings and theories change our view of memory function with age?

## Theories of Aging and Memory

Cognitive aging theories of memory are typically based on single-mechanism constructs, and the complexity of neuroimaging data does not readily map onto these theories. Nevertheless, some behavioral constructs and mechanisms are more successfully instantiated in the imaging literature than others. Theories of resource, such as views that suggest that decreases in speed of processing account for declines in fluid cognition with age (Salthouse, 1996), cannot directly account for the patterns of neural activation that occur with declines in memory performance in older adults. At present, the proposed causes of declines in speed with age are decreases in white matter integrity, dopamine receptors, and demyelination of axons (see Park et al., 2001, for a review). To support a view that speed changes are causal for age-related cognitive decline, it would be important to directly link decreased speed to these specific changes in the brain and then map these changes to memory function. This is an obviously tall order, and at this stage of development in the imaging literature, more proximal linkages between mechanisms and neural activations may be established more readily.

A simple version of the processing resource hypothesis accounting for age-related decline in memory (Park et al., 1996, 2002) is clearly problematic, but more complex versions of the working memory hypothesis may prove viable. In a simple form, it might be expected that availability of processing resources are reflected in level of activation of neural tissue. We have presented a number of studies indicating not only that sometimes lower functioning older adults, who presumably have less cognitive resource, show more activation (as in figure 1 in Lustig et al., 2003; Daselaar,

Veltman, Rombouts, Lazeron, et al., 2003; Logan et al., 2002, Stebbins et al., 2002), but also that older adults who are higher functioning show more activation (Cabeza et al., 2002; Rosen et al., 2002; Daselaar, Veltman, Rombouts, Lazeron, et al., 2003). Given these opposite patterns of findings, it is not possible that a simple mapping of activation levels to working memory capacity or speed of processing will be fruitful.

A more fertile approach may be to determine structures that are jointly or uniquely activated across tasks and/or categories of subjects (e.g., good or poor performers). As an example of this approach, Cabeza et al. (2004) examined activation patterns common to attention, working memory, and long-term memory. They reported that increases in prefrontal and parietal activations and decreases in hippocampal activations occurred with age across three different classes of tasks that tapped attention, working memory, and long-term memory, respectively. This particular finding suggests that increases in shared cross-task frontal, but not hippocampal, activation may be an important marker of cognitive resource with age. More studies are needed that examine broad classes of tasks or stimuli within the same subjects to secure a broader understanding of the relationship between neural activation in specific structures and performance.

Although the studies we presented in this chapter do not provide direct mapping to resource theories of memory, some findings map nicely onto inhibition theory. This view suggests that faulty inhibitory processes with age would result in increased neural activation when younger adults might show deactivations. There are several findings suggesting that older adults with the poorest memories (such as the patients with Alzheimer's disease depicted in figure 9.1b) show higher levels of neural activation, but as mentioned here, this does not necessarily mean that increased activation is dysfunctional, particularly because other studies show high-performing subjects sometimes show more activation. We also note that, despite the centrality of the construct of inhibition in cognitive aging (Hasher & Zacks, 1988; Zacks & Hasher, 1997), strong links in the behavioral literature between measures of inhibition and explicit memory have not been demonstrated. It may be, however, that neuroimaging may provide critical data connecting heightened activation to poor memory function with age, further establishing this view of cognitive aging.

Although the data are sparse, the neuroimaging literature does provide some confirmatory evidence that older adults' particularly poor source memory is mirrored in lower levels of neural activations for source compared to item memory (Cabeza et al., 2000). What remains to be established is that those older adults who show particularly large activation differences for source compared to item memory will also have the poorest item memory. The idea here would be that inefficient processing of, or decreased sensitivity to, contextual information reflects decrements in global memory function because source failures result from engaging fewer perceptual and reflective processes at encoding (Johnson, Hashtroudi, & Lindsay, 1993).

Finally, theories positing that older adults' memory function is more driven by familiarity than that of young adults (Jennings & Jacoby, 1993, 1997) have only begun to be tested at the neural level. Cabeza et al. (2004) proposed their finding of increased parahippocampal and decreased hippocampal activations in old relative to young adults could potentially be evidence for increased reliance on familiarity be-

cause that trace is less affected by aging than recollection. Findings of hippocampal/prefrontal distinctions in memory processes are also reminiscent of Jacoby's theory, with medial temporal activations reflecting automatic judgments of memory, and prefrontal activations indicating effortful strategic memory processes (Moscovitch & Winocur, 1992). Such a view would seem to suggest that older adults have less prefrontal involvement in retrieving memories, showing overall lower levels of activation in this area, and conceivably relying more strongly on hippocampal activations. Although the findings in the present review have been largely suggestive of decreased hippocampal function with age, Maguire and Frith's (2003) finding that older adults had greater hippocampal engagement for stimuli associated with their personal lives would seem to support the view that older adults rely more strongly on familiarity in making memory judgments.

### Neuroimaging Findings and Memory Theories

We now question how neuroimaging findings are changing theories of memory. At present, we would argue that neuroimaging findings are used as confirmatory data for extant behaviorally based theories of memory. That is, as behavioral theories are proposed, elaborated, and revised, they now must be able to accommodate neuroimaging findings because a failure to do so would indicate an inadequate theory or framework. At the same time that behavioral theories are evolving to accommodate neuroimaging findings, we also see evidence that particular interest is directed toward developing theories of memory plasticity and change in late adulthood, and we are seeing increased interest as well in interventions to improve memory and neural function (Logan et al., 2002). Memory theories are under development based on notions of compensation (Cabeza, 2002).

Given this new extraordinary ability to measure change and remodeling of neural organization with age that has resulted from imaging tools, we expect that theories of memory will increasingly be revised to integrate mechanisms of change or improvement in function in late adulthood as a result of training, contextual manipulations, or stimulation. Even from the relatively sparse and contradictory literature presented in this review, it is abundantly clear that the relatively static decline functions that occur in long-term memory across the life span are not mirrored in a pattern of linear decline in neural activation across an array of brain structures thought to be associated with memory.

Neuroimaging findings have also reinvigorated research that addresses hypotheses suggesting memory function can be broadly trained (Kramer & Willis, 2002), that cognitive vitality can be enhanced through exercise (Colcombe & Kramer, 2003), and that cognitive and social engagement facilitate a healthy mind (Schooler & Muluat, 2001). Because tools are at last available that provide sensitive measurement of neural function, we believe that studies of patient groups with affected memory function (e.g., from Alzheimer's disease, Parkinson's disease) will provide new insight into models of normal memory function in late adulthood.

Finally, we are convinced that the complex patterns of findings in the neuroimaging literature can only be understood through the study of individual differences along with studies that systematically manipulate variables that increase or decrease

difficulty of encoding in a systematic fashion. This will permit subjects to be categorized according to behavioral patterns of function (e.g., Glisky, Polster, & Routhicoux's 1995 battery for characterizing subjects in terms of frontal and hippocampal function) as well as neural patterns, such as bilaterality (Cabeza, 2002) or decreased neural selectivity (Logan et al., 2002; Park et al., in press).

Despite the many concerns we have expressed regarding interpretation of results from the neuroimaging literature, neuroimaging techniques have provided remarkable excitement and stimulation for the study of aging and memory. Memory theorists have fertile new ideas for development and measurement of conceptual models. We predict that cognitive neuroscience will be the dominant perspective from which theories of aging and memory evolve over the next decade.

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